



Study of Sensitivity of Angiosclerosis for Normotensive Offspring with Hypertensive Parents

*Xiaoli Liao

Henan Huaxia Esti Biotech Co., Ltd.
Room 1308, Building 5, R&D, No. 11 Changchun Road, Zhengzhou High tech Zone

*First and Corresponding author E-mail : liao1037392291@126.com

Abstract: In this observational study, we predicted the risk of having angiosclerosis for normotensive offspring with hypertensive parents in our customers via use of E-cardiac to measure the arterial stiffness, while E-Cardiac is one of the products of our company. A total of 1000 normotensive subjects (514 men and 486 women) aged 30 to 50 years (mean age 43 ± 3 years) were consent by writing to provide the measurement data for this investigation from the year 2015 to 2023. The measured pulse wave velocity higher than 1200 cm/s was coded R =1 as having the risk of angiosclerosis for the subject, otherwise coded R =0. A Logistic regression model was constructed to estimate the probability of the occurrence of R=1 for normotensive offspring with the age of over 45 years old and hypertensive parents. However, the model sensitivity revealed at the classification cut-off point 0.15 with the accuracy was 40% only. We concluded that the angiosclerosis may not be determined via inheritance from the hypertensive parents.

[Xiaoli Liao. **Study of Sensitivity of Angiosclerosis for Normotensive Offspring with Hypertensive Parents.** *Life Sci J* 2024;21(4):44-51]. ISSN 1097-8135 (print); ISSN 2372-613X (online). <http://www.lifesciencesite.com>. 06. doi:[10.7537/marlsj210424.06](https://doi.org/10.7537/marlsj210424.06).

Keywords: Study; Sensitivity; Angiosclerosis; Normotensive; Offspring; Hypertensive; Parents

Introduction

Most of the time, parental hypertension is associated with angiosclerosis for the offspring [1, 2]. The researchers reported that angiosclerosis measured by higher carotid-femoral pulse wave velocity might be heritable and have a genetic determinant [3]. Italian twin studies have also elucidated the genetic effects of arterial stiffness naturally [4]. The association between angiosclerosis and parental hypertension led to the concern about inherited angiosclerosis [5-8] but remains unclear [9-15].

By use of E-cardiac analysis is a promising, simple, non-invasive technique with similar effectiveness, repeatability, and accuracy compared to carotid-femoral pulse wave velocity measurement results to assess arterial stiffness [16-18]. In this observational study, we used the shape variation of the pulse wave to present the arterial stiffness for the subjects. The objects were focused on (1) the observation of uncertainty of the risk of angiosclerosis and (2) exploring the impacts of eligible predictors for normotensive offspring [19, 20].

Materials and methods

Study population

At baseline, since 2015, we have conducted a promotional customer value survey regarding E-cardiac customer services. We recruited the follow-up participants (30-50 years old, n= 1500) who had undergone measurement for three or more years. Participants with prevalent hypertension, cardiovascular disease and missing values of physical exam variables were removed. A total of screened 1000 (514 men and 486 women) individuals were referred for the primary analysis in this observational study. This study was a long-term survey of the satisfactions of using E-cardiac that can help us to know about the function and the customer value of the E-cardiac.

Survey collection

Survey was collected by the structured follow up questionnaires. Covariates included G (Gender), A (Age), BMI (Body Mass Index), HTM (Hypertensive mother), HTF (hypertensive

father), HTP (Hypertensive parents) and self-blood-pressure.

Blood pressure measurement

Blood pressure (BP) was obtained on the right arm of the participants in the sitting position, using an automated measurement device DB62 E-Cardiac according to current guidelines [21]. The mean of the three BP measurements was used for this analysis. Hypertension (SBP \geq 140 mmHg and/or diastolic BP (DBP) \geq 90 mmHg) was diagnosed by self-measurements. The data were collected via the APP system. However, hypertensive subjects were eliminated. All the subjects without hypertension were categorized as normotensive group in this study.

Arterial stiffness measurement

Our developed app can be used to assess arterial stiffness [22]. DB62 is used to provide timing markers. Time difference ΔT (s) was identified as the time interval between the wave front of the brachial waveforms. The path length is hypothesized via the rate of heart beat. $V = (L_a - L_b) / \Delta T$, $L_b = 0.2195 \times \text{height} - 2.0734$ and $L_a = 0.8129 \times \text{height} + 12.328$ [23]. The BP (blood pressure) determined by the Oscillo metric sensor and the heart rate were simultaneously recorded during the measurement.

Logistic Regression Analysis

Logistic regression can be used as a predictive analysis tool [24, 25]. In this study, we defined the event R=1 as the case of having risk of high-risk of angiosclerosis ($V \geq 1400$ cm/sec) and the predictors that may impact the event include G, A, HTM, HTF, HTP, BP and BMI. However, if a predictor could not be significant, it would be removed. The object of this study was to check if a subject could be inherited the risk of angiosclerosis from his (or her) hypertensive parent. Using R as the dichotomous criterion variable with covariate variables, a Logistic regression analysis was performed. Eliminating of non-significant predictors, predictive probability of target event R=1 for normotensive subject with covariate HTM, G and A was revealed. Two-tailed P-value ≤ 0.005 was a strict

criterion for analysis being performed by IBM SPSS 22 (IBM Inc, Chicago, IL, USA). Via the logistic regression analysis, the predictive probability of the R=1 can be estimated.

$$\ln(\text{odd}) = \beta_0 + \beta_1 \times G + \beta_2 \times A + \beta_3 \times \text{HTM} \quad (1)$$

Substituting the β values into the equation (1), we can get

$$\ln(\text{odd}) = -2.824 + 1.074 \times G + 0.4 \times A + 0.478 \times \text{HTM} \quad (2)$$

where odd is defined as $\frac{y}{1-y}$ and y is the predictive probability of the event of R=1, we can compute

$$y = \frac{\text{odd}}{1 + \text{odd}} \quad (3)$$

From equation (1) to equation (3), we can determine y as the predictive probability of the event R=1 for the subjects.

Most researchers tend to use higher cutoff point at least 0.4 to determine the most appropriate sensitivity. But when we deal with the binary predictor, we can accept the sensitivity value at smaller cutoff. Tabachnick and Fidell (2013) suggested using cutoff points as 0.32 (poor), 0.45 (fair), 0.55 (good), 0.63 (very good) or 0.71 (excellent) [26]. Causal inference requires two components: a model for expressing causal knowledge and a mechanism for processing the model [27]. The causal inference can thus be explained as independent variable causes the dependent variable to respond when independent variable changes. In this study, since sensitivity is the feature of the probability of occurrence of an effect that affects the causality, sensitivity can associate with both causality and effect via binary logistic analysis.

Results and discussion

In **Table 1**, P-values of predictors for logistic analysis were listed. Only A (age), G (gender) and HTM (hypertensive mother) were eligible under criteria of $p \leq 0.005$ [28]. Taking measurement of V via the DB62 E-cardiac as a dichotomous criterion variable R, we constructed a binary logistic regression model for A, G, and HTM. Beta coefficients of the binary regression analysis are listed in **Table 2**.

Table 1. List of significance of the variables in logistic analysis

Predictor	Significance
Age	0.000
Gender	0.000
HTM (hypertensive mother)	0.003
HTP (hypertensive parents)	0.078
HTF (hypertensive father)	0.219
HDL (high-density lipoprotein)	0.221
BMI (body mass index)	0.927

Table 2. β coefficients and odds ratio of predictors

Predictor ^a	β	df	Sig.	O.R. ^b	95% C.I. for O.R.	
					Lower	Upper
A	0.4	1	0.015	1.492	1.08	2.062
G	1.074	1	0.000	2.926	2.118	4.041
HTM	0.478	1	0.003	1.613	1.179	2.207
Constant	-2.824	1	0.000	0.059		

^a: the predictors and events are all coded in binary.; ^b: O.R.=EXP(β)

In this study, sensitivity measures the percentage accuracy of the occurrence of R=1 and specificity measures the percentage accuracy of the occurrence of R=0. The predictive probability was calculated via the equation (1) to (3). G=1 presents a male and G=0 a female. A=1 presents the age \geq 45 years old and A=0 is the age<45 years old. HTM=1 presents offspring has a hypertensive mother and HTM=0 for a normotensive mother.

In **Table 3**, the predictive probability of the occurrence of R=1 is demonstrated for normotensive offspring and it is shown that when the cutoff point was over 0.4, the sensitivity equals to zero and the specificity equals to 1, which means the accuracy of the probability to observe the occurrence of R=1 for the subjects with specific status of covariate predictors is zero. Status of covariate predictors impacted accuracy to predict the event of occurrence of R=1. The cutoff value of point 0.15 provided 39% accuracy (sensitivity) for classification of the occurrence of R=1. However, the predictive probability of R=1 is not affected by cutoff values. As a matter of fact, when the percentage accuracy of the prediction is zero, it is no sense to do any prediction. As we know, cutoff value means that a case is classified into the occurrence of the event when the predictive probability exceeds or equals the cutoff value; otherwise, it is classified into non-occurrence of the event. It was also realized that β coefficients would not be affected by classification cutoff. Nevertheless, cutoff impacts the sensitivity [29].

Table 3. Sensitivity and predictive probability of the predictors

				sensitivity				specificity			
cut off point				0.15	0.2	0.3	0.4	0.15	0.2	0.3	0.4
binary predictors status*				0.39	0.31	0.06	0.0	0.80	0.85	0.98	1.0
G	A	HTM	Probability								
1	1	1	29%								
1	0	1	22%								
0	1	0	21%								
1	0	0	15%								
0	1	1	13%								
0	0	1	9%								
0	1	0	8%								
0	0	0	6%								

*: G=1 for male; G=0 for female; A=1 for age ≥ 45 years old; A=0 for age < 45 years old; HTM=1 for hypertensive mother; HTM=0 for normotensive mother; Probability means for predictive probability of the occurrence of event R=1 ($V \geq 1400$ cm/s measured by DB2 E-Cardiac)

The probabilities of predicting the occurrence of R=1 with different sensitivities and specificities are presented in **Table 4**. Predictive probability of sample subjects having angiosclerosis ($V \geq 1400$ cm/s) with hypertensive mother could be estimated via the Logistic regression analysis. Sensitivity explains a predictor that may or may not result in changing the predicted probability of the occurrence of target event. Predictor and target event can be a causal inference of each other. Based on causal inference, previous studies use the commonality of twins to remove the effects of causal swaps, making the results unreliable [4].

Since cutoff threshold analysis has become a widely used data mining technique in many research and application fields, for example, to predict the activity or toxicological properties of untested chemicals to predict the carcinogenicity of rodents [30], the predictors of age (A), gender (G) and hypertensive mother (HTM) significantly influence the likelihood of the occurrence of events. From our analysis, the predictive probability of increased arterial stiffness (R=1) for normotensive offspring with a hypertensive mother is about 29%.

Table 4. Sensitivity and specificity of the predictors for R=1

Predictors	cutoff	Sensitivity	1 - Specificity
HTM	0.00	1.000	1.000
	.50	.362	.272
	1.00	0.000	0.000
A	0.00	1.000	1.000
	.50	.319	.233
	1.00	0.000	0.000
G	0.00	1.000	1.000
	.50	.720	.472
	1.00	0.000	0.000

In **Table 5**, though we only have 39% accuracy to predict the occurrence of R=1 at the cutoff point of 0.15, the accurate predictive rate of the occurrence of R=0 at cutoff point of 0.15 is approximately 80%. We can thus take parts of the effect caused by the predictor as another event. For a new event, the probability can be calculated.

For the target event of R=1, the sensitivity means percentage accuracy that was varied due to the predictive probability of the occurrence of R=1 and the specificity means percentage accuracy of the nonoccurrence of R=1. Meanwhile, for the target event of R=0, the sensitivity means percentage accuracy that was varied due to the predictive probability of the occurrence of R=0 and the specificity means percentage accuracy of the nonoccurrence of R=0.

Table 5. Sensitivity and specificity of the predictors at cutoffs

Event	Predictor	Cutoff	Sensitivity	Specificity
R=1	HTM	0.5	0	1
		0.4	0.36	0.765
		0.3	1	0
	A	0.3	1	0
		0.32	0.288	0.723
		0.35	0	1
	G	0.8	0	1
		0.7	0.678	0.466
		0.6	1	0
R=0	HTM	0.5	0	1
		0.4	0.565	0.485
		0.3	1	0
	A	0.3	1	0
		0.32	0.505	0.464
		0.35	0	1
	G	0.8	0	1
		0.7	0.749	0.291
		0.6	1	0

In **Table 6**, based on the characteristics of sensitivity analysis, we optimize the cutoff value points for events of R=1, G=1 and HTM=1 to get more reasonable prediction probability in logistic regression through the consideration of causal inference [31]. Causal inference may impact the change of the predictive probability for different target event at different conditions. Comparisons of the significance of predictors of Gender, R and HTM, the predictor AGE was removed for poor P-value (>0.005). At cutoff point of 0.25, it provides 64% accuracy that 33% by chance that a male subject with the high-risk of angiosclerosis would have a hypertensive mother. But at cutoff point of 0.7, it provides 68% accuracy that 64% by chance that a subject having both hypertensive mother and high-risk of angiosclerosis would be a male. Through the discussion of causal inference, at cutoff point 0.2, only 23% accuracy was observed for a normotensive male subject with hypertensive mother, 24% by chance (predictive probability) could have the high-risk of increased arterial stiffness, which is insufficient to support the

previous findings shown that more than 60% probability (odd>1.5) of normotensive offspring have the hereditary nature of hypertensive parents [3].

Table 6. Logistic regression analysis for causal inference

HTM=1 and G=1	Predictive Probability of R=1	At Cutoff point of 0.2	
	0.24	Sensitivity	Specificity
		0.23	0.88
HTM=1 and R=1	Predictive Probability of G =1	At Cutoff point of 0.7	
	0.64	Sensitivity	Specificity
		0.68	0.47
G=1 and R=1	Predictive Probability of HTM=1	At Cutoff point of 0.25	
	0.33	Sensitivity	Specificity
		0.64	0.43

A predict model of having increased arterial stiffness for the subjects was constructed by the sensitivity characteristics of the covariate predictors gender, age and hypertensive mother. 39% accuracy by chance to observe the occurrence of increased arterial stiffness for subjects at cutoff 0.15, which is even less than making a random guess for the event. In other word, less than 11% ($0.39 \times 0.29 = 0.11$) by chance that a male offspring with age older than 45 years old and hypertensive mother can have $V \geq 1400$ cm/s trait for the high-risk of angiosclerosis. The probability is truly low. According to our analysis, causal inference may help us to recognize that a subject having the probability of both increased arterial stiffness and hypertensive mother would be over 64% by chance to be observed, meanwhile this target event occurred of 68% probability correctly being assured that the subject is a male, at least, this finding is higher than the probability of a random guess. However, this result does not help too much determine of angiosclerosis being inherited from hypertensive mother.

Understanding the sensitivity of features of the predictors in this study does not provide information about which genes or environmental impacts are involved, or their importance in determining characteristics. Our sensitivity calculations are only used to express the variation ratio of hypertensive mother, age and gender would affect the high-risk of angiosclerosis via the measurements of $V (\geq 1400$ cm/s). Specifically, the proposed model we have established is to identify the characteristics of considering hypertensive mother in cross sectional statistical

analysis of the risk of angiosclerosis. Long-term observations to estimate the main source of bias in heritability should still depend on the features of blood biochemical tests and the scale of interactions of these factors, as well as disease diagnosis [32]. Our cross-sectional estimation is only used to understand the effects of hypertensive mother may impact the occurrence of having high risk of Angiosclerosis being determined by E-cardiac measurement significantly and co-affected by age and gender. A possible explanation may be related to the result from Anglo-Cardiff Collaborative Trial (ACCT), which is that pulse wave velocity is increased rather later in life (≥ 45 years) as well [33, 34].

This study enabled us to evaluate data on a large selected sample of individuals without environmental variability even we still must take the cutoff at 15% for the sensitivity analysis. Participants were all recruited from regular customers with similar lifestyles and dietary habits, which reduced the environmental confounders. Several limitations of the present study must be acknowledged. First, in developing countries like China, large sections of the community remain undiagnosed cardiac diseases and therefore the accuracy of self-reported family history would become a challenge. Another limitation was the cross-sectional nature of the study and the usefulness of family history in risk prediction, which should be tested in larger prospective studies. In addition, our study sample comprised relatively healthy young to middle aged community dwelling individuals of Chinese population in Zhengzhou city, which were

limited the generalizability of our observations to other age groups and ethnicities.

Conclusions

The use of logistic regression analysis can be effective and feasible for the study of causality. The dominant paradigm should be the activity of simulating nature, not the activity of the experimenter. Contrary to the paradigm of conservative statistics, we started with the relationships we knew in advance. Based on the logistic regression analysis that we have enough relationships to judge how predictor works, we clearly defined whether the events we are interested in meet empirical data and estimate them based on logistic regression relationships [31-34].

Our analysis has shown that a subject could be only predicted 39% correctly to be a male over the age of 45 years old with history of hypertensive mother. He has 29% by chance of having both angiosclerosis ($V \geq 1400$ cm/s) and hypertensive mother. For normotensive offspring, this possibility should not be neglected clinically. However, it does not provide sufficient evidence to support the genetic characteristics of having the risk of increased arterial stiffness with hypertensive mother because of low accurate predictive rate. This study provided evidence against previous studies.

Checking from different point of view, as different findings can be explained by different perspectives of causal inference, a subject both having the high-risk of angiosclerosis and hypertensive mother by regression analysis was speculated of 64% by chance is male and correctly predicted of 68% by chance of the occurrence to assure the subject is a male at the 0.7 cutoff point. Those observations and estimations may not be sufficient to support a normotensive male subject is inherited from a hypertensive mother to obtain the high-risk of angiosclerosis because of the crux of the problem is that the proportion of subjects with both risk of angiosclerosis and hypertensive mother in the population is too low. Conclusively, we were unable to see enough causal evidence of the heritability of the high-risk of angiosclerosis with hypertensive mother for normotensive offspring.

Conflicts of interest :

There are no conflicts of interest

References

1. Chu C, Dai Y, Mu J, Yang R, Wang M, Yang J, et al. Associations of risk factors in childhood with arterial stiffness 26 years later: the Hanzhong adolescent hypertension cohort. *J Hypertens* 2017, 35(Supplement 1):S10-S15.
2. Kozeta M, Nienke E. B, Hanneke B, Albert H, Eric A. P. S, Romy G, et al. Associations of Maternal and Paternal Blood Pressure Patterns and Hypertensive Disorders during Pregnancy with Childhood Blood Pressure. *J Am Heart Assoc* 2016, 5(10):1-18.
3. Andersson C, Quiroz R, Enserro D, Larson MG, Hamburg NM, Vita JA, Association of parental hypertension with arterial stiffness in nonhypertensive offspring: The Framingham Heart Study. *Hypertension* 2016, 68:584-589.
4. Medda E, Fagnani C, Schillaci G, Tarnoki AD, Tarnoki DL, Baracchini C, et al. Heritability of arterial stiffness and carotid intima-media thickness: an Italian twin study. *Nutr Metab Cardiovasc Dis* 2014, 24:514-517.
5. Roman S, Copenhaver M, Long-Term Effects of Childhood Risk Factors on Cardiovascular Health During Adulthood. *Clin Med Rev Vasc Health* 2015, 7:1-5.
6. Yang L, Yinkun Y, Xiangjun Y, Shengxu L, Lydia B, Jiang H , et al. Long-Term Burden of Higher Body Mass Index and Adult Arterial Stiffness Are Linked Predominantly Through Elevated Blood Pressure. *HYPERTENSION* 2018, 73:229-234.
7. Masaki O, Fumiaki N, Terunaga M, Kobayashi Y, Association between novel arterial stiffness indices and risk factors of cardiovascular disease. *BMC Cardiovasc Disord* 2016, 16(211):1-7.
8. Wang NY, Young JH, Meoni LA, Ford DE, Erlinger TP, Klag MJ, et al. Blood pressure change and risk of hypertension associated with parental hypertension: The Johns Hopkins Precursors Study. *Arch Intern Med* 2008; 168:643-648.
9. Gottsäter M, Epidemiological, mechanistic and genetic aspects of vascular ageing and arterial stiffness in the population. Lund University, Department of Clinical Sciences; 2017.
10. Liao D1, Arnett DK, Tyroler HA, Riley WA, Chambless LE, Szklo M, et al. Arterial stiffness and the development of hypertension: the ARIC Study. *Hypertension* 1999, 34:201-206.
11. Niki K, Erietta K, Sotirios D, Petros D, Anna-Bettina H, Vasilios G. A, et al. Is There an Association Between Carotid-Femoral Pulse Wave Velocity and Coronary Heart Disease in Patients with Coronary Artery Disease: A Pilot Study. *The Open Cardiovascular Medicine Journal* 2016, 10:64-68.
12. Parikh NI, Pencina MJ, Wang TJ, Benjamin EJ, Lanier KJ, Levy D, et al. A risk score for

- predicting near-term incidence of hypertension: the Framingham Heart Study. *Ann Intern Med* 2008; 148:102-110.
13. Tebi El, Baligh E, Gamal H, Ashour Z, Youssef G, Shahata A, Familial history of hypertension as a predictor of increased arterial stiffness. *Eur Heart J* 2013, 34 (suppl):5003.
 14. Yasmin, Rosalba F, Brown MJ, Determinants of Arterial Stiffness in Offspring of Families with Essential Hypertension. *AJH* 2004, 17(292–298).
 15. G DB, Epidemiology and prevention of cardiovascular disease: Quo vadis? *Eur J Prev Cardiol* 2017, 24(7):768-772.
 16. Shoko T, Tetsuo S, Eiji K, Kayo S, Sawako H, Hidenori K, et al. Brachial-ankle Pulse Wave Velocity as an Index of Central Arterial Stiffness. *Journal of Atherosclerosis and Thrombosis* 2010, 17(6):1-8. 1.
 17. Tanaka H, Munakata M, Kawano Y, Ohishi M, Shoji T, Sugawara J, et al. Comparison between carotid-femoral and brachial-ankle pulse wave velocity as measures of arterial stiffness. *J Hypertens* 2009, 27.:2022-2027.
 18. Hyung-Suk L, Hye Lim L, Ho-seong H, Minju Y, Ji Seon K, Sung-Hyun L, et al. Clinical usefulness of ankle brachial index and brachial-ankle pulse wave velocity in patients with ischemic stroke. *J Biomed Res* 2016, 30(4):285-291.
 19. Jianjun M, Shuhui Z, Qiufang L, Fuqiang L, Zhiqian L, Evolution of blood pressure from adolescents to youth in salt sensitivities: a 18-year follow-up study in Hanzhong children cohort. *Nutrition Journal* 2012, 11 (70).
 20. Moussa MMM, RIE-m, El-Ezaby HH, Prevalence of hypertension and associated risk factors among university students: Comparative study. *Journal of Nursing Education and Practice* 2016, 6(5):19-27.
 21. Jordana B. Cohen, Tiffany C. Wong, Bruce S. Alpert, Townsend RR: Assessing the Accuracy of the Omron HEM-907XL Oscillometric Blood Pressure Measurement Device in Non-Dialytic Chronic Kidney Disease Patients. *J Clin Hypertens* 2017, 19(3):296-302.
 22. Shoko T, Tetsuo S, Eiji K, Kayo S, Sawako H, Hidenori K, et al. Brachial-ankle Pulse Wave Velocity as an Index of Central Arterial Stiffness. *Journal of Atherosclerosis and Thrombosis* 2010, 17(6):1-8.
 23. Hyung-Suk L, Hye Lim L, Ho-seong H, Minju Y, Ji Seon K, Sung-Hyun L, et al. Clinical usefulness of ankle brachial index and brachial-ankle pulse wave velocity in patients with ischemic stroke. *J Biomed Res* 2016, 30(4):285-291.
 24. Steven F, (2014). *Predictive Analytics, Data Mining and Big Data. Myths, Misconceptions and Methods*. Basingstoke: Palgrave Macmillan. ISBN 978-1-137-37927-6.
 25. Phillip B P, Dennis G O'C, Endowed S-L, Regression Analysis for Prediction: Understanding the Process. *Cardiopulm Phys Ther J* 2009, 20(3):23-26.
 26. Barbara G Tabachnick, Fidell LS, *Using Multivariate Statistics*. Boston: Pearson Education; 2013.
 27. Pearl J, Causal inference in statistics: An overview. *Statistics Surveys* 2009, 3: 96-146.
 28. Swets JA, Measuring the accuracy of diagnostic systems. *Science* 1988; 240(4857): 1285-1293.
 29. Sperandei S, Understanding logistic regression analysis. *Biochemia Medica* 2014, 24(1):12-18.
 30. Ross D. K, Ashwin S, and Luc D, 'Warmr: A Data Mining Tool for Chemical Data', *Journal of Computer-Aided Molecular Design*, 15 (2001), 173-81.
 31. Kailash B, Vreeken J, ORIGO: causal inference by compression. *Knowledge and Information Systems* 2018, 56(2):285-307.
 32. Henok A, Frew T, Ermias B, 'Prevalence and Associated Factors of Hypertension among Adults in Ethiopia: A Community Based Cross-Sectional Study', *BMC Res Notes*, 10 (2017), 1-8.
 33. Carmel M. Mc, Yasmin M-PK, Ian R. H, Ahmad Q, Ian B. W, John R. Cockcroft, 'Normal Vascular Aging: Differential Effects on Wave Reflection and Aortic Pulse Wave Velocity the Anglo-Cardiff Collaborative Trial (Acct)', *Journal of the American College of Cardiology*, 46 (2005), 1753-60.
 34. McEniery CM, Yasmin M-PK, McDonnell BJ, Munnery M, Hickson SS, Franklin SS, et al. The impact of cardiovascular risk factors on aortic stiffness and wave reflections depends on age: the Anglo-Cardiff Collaborative Trial (ACCT III). *Hypertension* 2010, 56(4):591-597.